Drug Coverage Policy

Effective Date……6/1/2025
Coverage Policy Number……IP0478
Policy Title……Amvuttra

Amyloidosis – Amvuttra

- Amvuttra™ (vutrisiran subcutaneous injection - Alnyam)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Amvuttra, a transthyretin (TTR)-directed small interfering RNA, is indicated for the following uses:[1]

- **Polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR),** in adults.
- **Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM),** in adults to reduce cardiovascular mortality, cardiovascular hospitalization, and urgent heart failure visits.

Disease Overview
ATTR is a progressive disease caused by variants in the TTR gene leading to multisystem organ dysfunction.[5] Although patients with ATTR may present with a variety of symptoms; neuropathy or cardiomyopathy are often the most prominent symptoms. Patients may also present with a mixed phenotype and exhibit signs of both neuropathy and cardiomyopathy.

Guidelines
There are no guidelines that include recommendations for Amvuttra. A scientific statement from the American Heart Association (AHA) on the treatment of the cardiomyopathy of hATTR amyloidosis (July 2020) includes recommendations related to polyneuropathy.[3] Canadian guidelines for the treatment of patients with polyneuropathy (February 2021) include treatment recommendations for hATTR polyneuropathy as well.[2,4] In general, Onpattro® (patisiran intravenous infusion) and Tegsedi® (inotersen subcutaneous injection) are recommended for patients with hATTR polyneuropathy.

For patients with hATTR amyloidosis with polyneuropathy, the AHA recommends treatment with Onpattro or Tegsedi.[3] For patients with hATTR with polyneuropathy and cardiomyopathy, Onpattro, Tegsedi, or Vyndamax® (tafamidis meglumine capsules)/Vyndaqel™ (tafamidis capsules) are recommended. Use of combination therapy is discussed; however, it is noted that there is little data to support combination therapy.

The American College of Cardiology expert consensus decision pathway on comprehensive multidisciplinary care for patients with cardiac amyloidosis (2023) recognizes tafamidis as a treatment option for ATTR-CM.[6] Early diagnosis is crucial since tafamidis slows the progression of the disease. It is noted that the benefit of tafamidis has not been observed in patients with New York Heart Association Class IV symptoms.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for prescription benefit coverage of Amvuttra. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Amvuttra as well as the monitoring required for adverse events and long-term efficacy, approval requires Amvuttra to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required where noted in the criteria. Documentation may include, but not limited to, chart notes, laboratory tests, medical test results, genetic test results, claims records, and/or other information.

Amvuttra is considered medically necessary when the following are met:

FDA-Approved Indication

1. **Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis (hATTR).** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient is ≥18 years of age; AND
   - **B)** Documentation provided that the patient has a transthyretin pathogenic variant as confirmed by genetic testing; AND
   - **C)** Documentation provided that the patient has symptomatic polyneuropathy; AND
     Note: Examples of symptomatic polyneuropathy include reduced motor strength/coordination, and impaired sensation (e.g., pain, temperature, vibration, touch).

Examples of assessments for symptomatic disease include history and clinical exam, electromyography, or nerve conduction velocity testing.

D) Patient does not have a history of liver transplantation; AND

E) The medication is prescribed by or in consultation with a neurologist, geneticist, or a physician who specializes in the treatment of amyloidosis.

Dosing. Approve the following dosing regimen (A and B):

A) The dose is 25 mg by subcutaneous injection; AND

B) The dose is administered not more frequently than once every 3 months.

2. **Cardiomyopathy of Wild-Type or Hereditary Transthyretin-Mediated Amyloidosis (ATTR-CM).** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   Note: Variant Transthyretin Amyloidosis is also known as Hereditary Transthyretin Amyloidosis.
   A) Patient is ≥ 18 years of age; AND
   B) Documentation provided that the diagnosis was confirmed by ONE of the following (i, ii, or iii):
      i. A technetium pyrophosphate scan (i.e., nuclear scintigraphy); OR
      ii. A tissue biopsy with confirmatory transthyretin (TTR) amyloid typing by mass spectrometry, immunoelectron microscopy, or immunohistochemistry; OR
      iii. Patient had genetic testing which, according to the prescriber, identified a transthyretin (TTR) pathogenic variant; AND
      Note: Examples of TTR variants include Val122Ile variant and Thr60Ala variant. If the patient has wild-type amyloidosis, this is **not** a TTR pathogenic variant.
   C) Diagnostic cardiac imaging has demonstrated cardiac involvement; AND
   Note: Examples of cardiac imaging include echocardiogram and cardiac magnetic imaging. Examples of cardiac involvement on imaging include increased thickness of the ventricular wall or interventricular septum.
   D) Patient has heart failure, but does **not** have New York Heart Association class IV disease; AND
   E) The medication is prescribed by or in consultation with a cardiologist or a physician who specializes in the treatment of amyloidosis.

   Dosing. Approve the following dosing regimen (A and B):
   A) The dose is 25 mg by subcutaneous injection; AND
   B) The dose is administered not more frequently than once every 3 months.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Amvuttra for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent use with other medications indicated for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy (e.g., Attruby [acoramidis tablets], Onpattro [patisiran intravenous infusion], Tegsedi [inotersen subcutaneous injection], Wainua [eplontersen subcutaneous injection], or a tafamidis product).**

The requested medication should not be administered in combination with other medications indicated for polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy. Combination therapy is generally not recommended due to a lack of controlled clinical trial data supporting additive efficacy.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J0225	Injection, vutrisiran, 1 mg

References

1. Amvuttra™ subcutaneous injection [prescribing information]. Cambridge, MA: Alnylam; February 2023.
2. Alcantara M, Mezi MM, Baker SK, et al. Canadian guidelines for hereditary transthyretin amyloidosis polyneuropathy management. *Can J Nero Sci.* 2022;49:7-18.
3. Kittleson MM, Maurer MS, Ambardekar AV, et al; on behalf of the American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology. AHA scientific statement: cardiac amyloidosis: evolving diagnosis and management. *Circulation.* 2020;142:e7-e22.
4. Adams D, Tournev IL, Talor MS, et al. Efficacy and safety of vutrisitan for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial. *Amyloid*. 2023; 30(1):1-9.
5. US Department of Health and Human Services, National Institutes of Health. Transthyretin amyloidosis. Available at: https://ghr.nlm.nih.gov/condition/transthyretin-amyloidosis#diagnosis. Accessed on March 21, 2025.
6. Kittleson M, Ruberg FL, Ambardekar AV, et al. A report of the American College of Cardiology Solution Set Oversight Committee. 2023 ACC expert consensus decision pathway on comprehensive multidisciplinary care for the patient with cardiac amyloidosis. *J Am Coll Cardiol*. 2023;81(11):1076-1126.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	**Polyneuropathy of Hereditary Transthyretin–Mediated Amyloidosis (hATTR).** **Removed** 'Documentation that other causes of neuropathy have been excluded (for example, diabetes)' **Updated** 'Documented diagnosis of hereditary transthyretin-mediated (hATTR) amyloidosis confirmed by a transthyretin *(TTR)* genetic variant	10/1/2024

	(pathogenic or likely pathogenic variant)' to 'Patient has a transthyretin pathogenic variant as confirmed by genetic testing' **Updated** 'Documentation of symptomatic polyneuropathy confirmed by history and clinical exam, electromyography, or nerve conduction velocity' to 'Patient has symptomatic polyneuropathy; Note: Examples of symptomatic polyneuropathy include reduced motor strength/coordination, and impaired sensation (e.g., pain, temperature, vibration, touch). Examples of assessments for symptomatic disease include history and clinical exam, electromyography, or nerve conduction velocity testing.' **Added** to dosing 'The dose is administered not more frequently than once every 3 months.' **Conditions Not Covered.** **Removed** (1) Treatment of Cardiomyopathy hATTR in the Absence of Polyneuropathy Symptoms, (2) Treatment of Polyneuropathy Not Related to hATTR Amyloidosis. **Updated** title from "Vutrisiran' to 'Amyloidosis – Amvuttra'	
Annual Revision	**Added "Documentation**: Documentation is required where noted in the criteria. Documentation may include, but not limited to, chart notes, laboratory tests, medical test results, genetic test results, claims records, and/or other information." **Polyneuropathy of Hereditary Transthyretin–Mediated Amyloidosis (hATTR)** **Updated** criteria **from** "Patient has a transthyretin pathogenic variant as confirmed by genetic testing" **to** "Documentation provided that the patient has a transthyretin pathogenic variant as confirmed by genetic testing." **Updated** criteria **from** "Patient has symptomatic polyneuropathy" **to** "Documentation provided that the patient has symptomatic polyneuropathy." **Conditions Not Covered** Concurrent use with other medications indicated for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis or transthyretin-mediated amyloidosis-cardiomyopathy (e.g., Attruby (acoramidis tablets), Onpattro (patisiran intravenous infusion), Tegsedi (inotersen subcutaneous injection), Wainua (eplontersen subcutaneous injection), or a tafamidis	3/1/2025

	product) was changed to as listed (previously, concomitant use with Onpattro [patisiran intravenous injection], Tegsedi [inotersen subcutaneous injection], Wainua [eplontersen subcutaneous injection, or a Tafamidis product was listed.)	
Annual Revision	**Cardiomyopathy of Wild-Type or Hereditary Transthyretin-Mediated Amyloidosis (ATTR-CM):** This condition and criteria for approval were added to the policy.	6/1/2025

The policy effective date is in force until updated or retired.